

# WEST Search History

DATE: Thursday, September 25, 2003

<u>Set</u>	<u>Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set</u>
side by side				result set
<i>DB=USPT; PLUR=YES; OP=ADJ</i>				
L32	L31 and L30		198	L32
L31	((435/7.21 )!.CCLS.))		1515	L31
L30	((435/4 )!.CCLS. )		2991	L30
L29	L20 and L23		0	L29
L28	L21 and L15		0	L28
L27	L21 and L25		0	L27
L26	L20 and L25		0	L26
L25	L23 and L24		13	L25
L24	activity		354143	L24
L23	(EC 2.3.1.57) or((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR PUTRESCINE OR DIAMINE OR (SPERMIDINE/SPERMINE)) Near5(N1-ACETYLTRANSFERASE)		13	L23
L22	NON near5((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR PUTRESCINE OR DIAMINE OR (SPERMIDINE/SPERMINE))near5(N1-ACETYLTRANSFERASE))		0	L22
L21	L19 and L20		2	L21
L20	amantadine		926	L20
L19	(polyamine analog) near5 (( spermidine/spermine) or spermine or spermidine)		20	L19
<i>DB=JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ</i>				
L18	L13 and L14		2	L18
L17	L13 and L15		1	L17
L16	L14 and L15		0	L16
L15	NON and((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR PUTRESCINE OR DIAMINE OR (SPERMIDINE/SPERMINE)) and(N1-ACETYLTRANSFERASE))		1	L15
L14	((body fluid) or plasma or serum or urine or blood)and (mammal or human) (EC 2.3.1.57) or((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR		31058	L14
L13	PUTRESCINE OR DIAMINE OR (SPERMIDINE/SPERMINE)) and(N1-ACETYLTRANSFERASE)		7	L13
<i>DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ</i>				
L12	L10 and L3		0	L12
L11	L10 and L2		0	L11
NON near5((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR				

L10 PUTRESCINE OR DIAMINE OR  
(SPERMIDINE/SPERMINE))near5(N1-ACETYLTRANSFERASE))

1 L10

DB=JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ

L9	L5 and L6	0	L9
L8	L4 and L6	0	L8
L7	L4 and L5	0	L7
L6	L1 and L2	1	L6
L5	L2 and L3	1	L5
L4	L1 and L3	1	L4
L3	((body fluid) or plasma or serum or urine or blood)near5 (mammal or human)	13473	L3
L2	amantadine or (acetyl amantadine)	102	L2
L1	PUTRESCINE OR DIAMINE OR (SPERMIDINE/SPERMINE)) Near5(N1-ACETYLTRANSFERASE)	7	L1

END OF SEARCH HISTORY

# The Contents of Case 10085051us09252003

Qnum	Query	DB Name
Q1	(EC 2.3.1.57) or((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR PUTRESCINE OR DIAMINE OR (SPERMIDINE/SPERMINE)) Near5(N1-ACETYLTRANSFERASE)	JPAB,EPAB,DWPI
Q2	amantadine or (acetyl amantadine)	JPAB,EPAB,DWPI
Q3	((body fluid) or plasma or serum or urine or blood)near5 (mammal or human)	JPAB,EPAB,DWPI
Q4	Q1 and Q3	JPAB,EPAB,DWPI
Q5	Q2 and Q3	JPAB,EPAB,DWPI
Q6	Q1 and Q2	JPAB,EPAB,DWPI
Q7	Q4 and Q5	JPAB,EPAB,DWPI
Q8	Q4 and Q6	JPAB,EPAB,DWPI
Q9	Q5 and Q6	JPAB,EPAB,DWPI
Q10	NON near5((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR PUTRESCINE OR DIAMINE OR (SPERMIDINE/SPERMINE))near5(N1-ACETYLTRANSFERASE))	USPT,PGPB,JPAB,EPAB,
Q11	Q10 and Q2	USPT,PGPB,JPAB,EPAB,
Q12	Q10 and Q3	USPT,PGPB,JPAB,EPAB,
Q13	(EC 2.3.1.57) or((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR PUTRESCINE OR DIAMINE OR (SPERMIDINE/SPERMINE)) and(N1-ACETYLTRANSFERASE)	JPAB,EPAB,DWPI
Q14	((body fluid) or plasma or serum or urine or blood)and (mammal or human)	JPAB,EPAB,DWPI
Q15	NON and(((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR PUTRESCINE OR DIAMINE OR (SPERMIDINE/SPERMINE)) and(N1-ACETYLTRANSFERASE))	JPAB,EPAB,DWPI
Q16	Q14 and Q15	JPAB,EPAB,DWPI
Q17	Q13 and Q15	JPAB,EPAB,DWPI
Q18	Q13 and Q14	JPAB,EPAB,DWPI
Q19	(polyamine analog) near5 (( spermidine/spermine) or spermine or spermidine)	USPT
Q20	amantadine	USPT
Q21	Q19 and Q20	USPT
Q22	NON near5((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR PUTRESCINE OR DIAMINE OR (SPERMIDINE/SPERMINE))near5(N1-ACETYLTRANSFERASE))	USPT
Q23	(EC 2.3.1.57) or((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR PUTRESCINE OR DIAMINE OR	USPT

((SPERMIDINE/SPERMINE)) Near5(N1-ACETYLTRANSFERASE)

Q24	activity	USPT
Q25	Q23 and Q24	USPT
Q26	Q20 and Q25	USPT
Q27	Q21 and Q25	USPT
Q28	Q21 and Q15	USPT
Q29	Q20 and Q23	USPT
Q30	((435/4)! .CCLS. )	USPT
Q31	((((435/7.21)! .CCLS.))	USPT
Q32	Q31 and Q30	USPT

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EC 2.3.1.57

Common name: diamine N-acetyltransferase

Reaction: acetyl-CoA + an alkane-diamine = CoA + an N-acetyldiamine

Other name(s): spermidine acetyltransferase; putrescine acetyltransferase; putrescine (diamine)-acetylating enzyme; diamine acetyltransferase; spermidine/spermine N<sup>1</sup>-acetyltransferase; spermidine N<sup>1</sup>-acetyltransferase; acetyl-coenzyme A-1,4-diaminobutane N-acetyltransferase; putrescine acetylase; putrescine N-acetyltransferase  
Connecting via Winsock to STN

=> e amantadine

E1 10 AMANTA/BI  
E2 9 AMANTAD/BI  
E3 9 -> AMANTADINE/BI  
E4 9 AMANTAN/BI  
E5 158 AMANTANE/BI  
E6 2 AMANTANEACETIC/BI  
E7 4 AMANTANEACET/BI  
E8 1 AMANTANEACETATE/BI  
E9 1 AMANTANEACETATE/BI  
E10 1 AMANTANEACETIC/BI  
E11 2 AMANTANEACETOBISCHLORO/BI  
E12 1 AMANTANEACETOBISCHLOROACET/BI

=> s e3

L1 9 AMANTADINE/BI  
E1 THROUGH E1 ASSIGNED

L2 1 352464-70-1/RN  
L3 1 L2

=> e acetyl amantadine

E2 1 ACETYKCYCLOHEXANONE/BI  
E3 96211 ACETYL/BI

=> index bioscience

=> ssat or spermine and acetyltransferase

5 FILE ADISCTI  
5 FILE ADISINSIGHT  
3 FILE AGRICOLA  
2 FILE AQUASCI  
1 FILE BIOBUSINESS  
167 FILE BIOSIS  
5 FILE BIOTECHABS  
5 FILE BIOTECHDS  
90 FILE BIOTECHNO  
17 FILE CABA  
81 FILE CANCERLIT  
156 FILE CAPLUS  
2 FILE CONFSCI  
75 FILE DDFU  
15 FILE DGENE  
87 FILE DRUGU  
7 FILE EMBAL  
130 FILE EMBASE  
99 FILE ESBIOBASE  
8 FILE FEDRIP  
53 FILE GENBANK  
10 FILE IFIPAT  
6 FILE JICST-EPLUS  
44 FILE LIFESCI  
44 FILES SEARCHED...

3 FILE MEDICONF  
145 FILE MEDLINE  
8 FILE NTIS  
60 FILE PASCAL  
24 FILE PROMT  
151 FILE SCISEARCH  
127 FILE TOXCENTER  
67 FILE USPATFULL  
2 FILE USPAT2  
8 FILE WPIDS  
8 FILE WPINDEX

L6 QUE SSAT OR SPERMINE AND ACETYLTRANSFERRASE, 35 FILES HAVE ONE OR MORE ANSWERS

L7 QUE ((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR PUTRESCINE OR DIAMINE OR (SPERMIDINE/SPERMINE)) (5N) (N1-ACETYLTRANSFERASE)32 FILES HAVE ONE OR MORE ANSWERS

L8 QUE NON (5N)((DIAMINE N-) OR SPERMIDINE OR PUTRESCINE OR PUTRESCINE OR DIAMINE OR (SPERMIDINE/SPERMINE)) (5N) (N1-ACETYLTRANSFERASE)4 FILES HAVE ONE OR MORE ANSWERS

L9 QUE L6 AND L7 26 FILES HAVE ONE OR MORE ANSWERS

L10, QUE AMANTADINE OR ACETYL AMANTADINE 56 FILES HAVE ONE OR MORE ANSWERS

L11 QUE L10(L) ANT/RL 1 FILES HAVE ONE OR MORE ANSWERS

L12 QUE L8 AND L11 1 FILES HAVE ONE OR MORE ANSWERS

L13 QUE (BODY FLUID OR PLASMA OR SERUM OR URINE OR BLOOD)(5N) (MAMMAL OR HUMAN ) 65 FILES HAVE ONE OR MORE ANSWERS

L14 QUE L8 AND L13 2 FILES HAVE ONE OR MORE ANSWERS

=> d rank

F1 1\* IFIPAT  
F2 1\* USPATFULL  
d.bib.abs L15 1-2

L15 ANSWER 1 OF 2 IFIPAT COPYRIGHT 2003 IFI on STN

AN 10188578 IFIPAT;IFIUDB;IFICDB

TI METHOD FOR ASSAYING NON-SPERMINE/SPERMIDINE ACTIVITY

OF SPERMIDINE/SPERMINE N1-ACETYLTRANSFERASE  
(SSAT); DETERMINING NON-SPERMINE/SPERMIDINE ACTIVITY

OF SPERMINE/SPERMIDINE N1-ACETYLTRANSFERASE  
IN MAMMAL; OBTAIN MAMMALIAN SAMPLE, SCREEN AND MEASURE AMOUNT OF  
ACETYLATED SUBSTRATE

INF Bras; Alvaro P., Winnipeg, CA  
Sitar; Daniel S., Winnipeg, CA

IN Bras Alvaro P (CA); Sitar Daniel S (CA)

PAF Unassigned

PA Unassigned Or Assigned To Individual (68000)

AG BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747,  
US

PI US 2002132280 A1 20020919

AI US 2002-85051 20020301

PRAI US 2001-272322P 20010302 (Provisional)

FI US 2002132280 20020919  
DT Utility; Patent Application - First Publication  
FS CHEMICAL  
APPLICATION  
CLMN 11  
GI 6 Figure(s).

FIG. 1 represents the metabolic disposition of amantadine (Adapted from Koppel and Tenczer (1985)) 1. Amantadine 2. NAcetylamantadine (major metabolite) 3. N-methylamantadine 4. N, N1-dimethylamantadine 5. N-methyleneamantadine 6. Nformylamantadine 7. and 8. possible stepwise oxidation of Ndimethylamantadine (4) 9. N-ethylideneamantadine 10. 1adamantol acetate.

FIG. 2 is a plot of urinary excretion of acetylamantadine by transgenic mice overexpressing SSAT and injected with amantadine HCl (3 mg/kg). Control non-transgenic mice undergoing the same procedures did not excrete acetylamantadine in their urine. The values reported are mean + -S.E. of 4 separate experiments.

FIG. 3 is a representative plot of V vs. S demonstrating spermidine acetylation by transgenic mouse liver 100,000 x g supernatant containing SSAT with apparent  $K_m = 263 \mu M$  and  $V_{max} = 0.010 \text{ nmol/min/mg protein}$  ( $r^2 = 0.99$ ). The addition of a therapeutic concentration (2.5  $\mu M$ ) of amantadine (A) causes inhibition of spermidine acetylation and an increase in the apparent  $K_m$  to 542  $\mu M$  and  $V_{max}$  to 0.014  $\text{nmol/min/mg protein}$  ( $r^2 = 0.99$ ).

FIG. 4 is a representative plot for the inhibition of acetyl spermidine production by increasing amantadine concentrations in the presence of 50  $\mu M$  spermidine. Spermidine acetylation is completely inhibited by 10,000  $\mu M$  amantadine.

FIG. 5A is a representative Dixon plot of 1/  $\epsilon$  versus (I), showing the inhibition of acetyl spermidine production by increasing amantadine (I) concentrations in the presence of 50  $\mu M$  and 200  $\mu M$  spermidine. The intersection of the two lines to left of y-axis and above the negative x-axis indicate the inhibition could be competitive or mixed inhibition.

FIG. 5B is a representative Cornish-Bowden plot  $S/v$  versus (I) of the same data as in FIG. 5A. The two parallel lines in the plot indicate competitive inhibition.

AB This invention relates to a method for assaying activity of the enzyme spermidine/spermine N1-acetyltransferase (SSAT) using SSAT substrates by detecting acetylated forms of the SSAT substrates. SSAT substrates may include amantadine wherein metabolism of amantadine occurs in part by the action of the inducible enzyme SSAT to produce the acetylated metabolite Nacetylamantadine.

CLMN 11 6 Figure(s).

FIG. 1 represents the metabolic disposition of amantadine (Adapted from Koppel and Tenczer (1985)) 1. Amantadine 2. NAcetylamantadine (major metabolite) 3. N-methylamantadine 4. N, N1-dimethylamantadine 5. N-methyleneamantadine 6. Nformylamantadine 7. and 8. possible stepwise oxidation of Ndimethylamantadine (4) 9. N-ethylideneamantadine 10. 1adamantol acetate.

FIG. 2 is a plot of urinary excretion of acetylamantadine by transgenic mice overexpressing SSAT and injected with amantadine HCl (3 mg/kg). Control non-transgenic mice undergoing the same procedures did not excrete acetylamantadine in their urine. The values reported are mean + -S.E. of 4 separate experiments.

FIG. 3 is a representative plot of V vs. S demonstrating spermidine acetylation by transgenic mouse liver 100,000 x g supernatant containing SSAT with apparent  $K_m = 263 \mu M$  and  $V_{max} = 0.010 \text{ nmol/min/mg protein}$

( $r^2=0.99$ ). The addition of a therapeutic concentration (2.5  $\mu$ M) of amantadine (A) causes inhibition of spermidine acetylation and an increase in the apparent  $K_m$  to 542  $\mu$ M and  $V_{max}$  to 0.014 nmol/min/mg protein ( $r^2=0.99$ ).

FIG. 4 is a representative plot for the inhibition of acetylspermidine production by increasing amantadine concentrations in the presence of 50  $\mu$ M spermidine. Spermidine acetylation is completely inhibited by 10,000  $\mu$ M amantadine.

FIG. 5A is a representative Dixon plot of  $1/\text{upsilon}$  versus ( $I$ ), showing the inhibition of acetylspermidine production by increasing amantadine ( $I$ ) concentrations in the presence of 50  $\mu$ M and 200  $\mu$ M spermidine. The intersection of the two lines to left of y-axis and above the negative x-axis indicate the inhibition could be competitive or mixed inhibition.

FIG. 5B is a representative Cornish-Bowden plot  $S/v$  versus ( $I$ ) of the same data as in FIG. 5A. The two parallel lines in the plot indicate competitive inhibition.

L15 ANSWER 2 OF 2 USPATFULL on STN

AN 2002:243094 USPATFULL

TI Method for assaying non-spermine/spermidine activity of spermidine/spermine N1-acetyltransferase (SSAT)

IN Sitar, Daniel S., Winnipeg, CANADA

Bras, Alvaro P., Winnipeg, CANADA

PI US 2002132280 A1 20020919

AI US 2002-85051 A1 20020301 (10)

PRAI US 2001-272322P 20010302 (60)

DT Utility

FS APPLICATION

LREP BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747

CLMN Number of Claims: 11

ECL Exemplary Claim: 1

DRWN 5 Drawing Page(s)

LN.CNT 667

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to a method for assaying activity of the enzyme spermidine/spermine N<sup>1</sup>-acetyltransferase (SSAT) using SSAT substrates by detecting acetylated forms of the SSAT substrates. SSAT substrates may include amantadine wherein metabolism of amantadine occurs in part by the action of the inducible enzyme SSAT to produce the acetylated metabolite N-acetylamantadine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.